Stereoselective Synthesis of Alcohols, XLVIII[1]

Linear Synthesis of (9*S*)-Dihydro-erythronolide A

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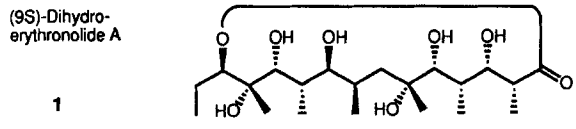
Received July 20, 1994

Key Words: Erythronolide A / Allylboration, stereoselective

Starting from building block **3** comprising the C-7 to C-15 segment of erythronolide A, a linear synthesis of erythronolide A has been achieved. Key steps were a Sharpless-epoxidation to set up the sterocenter at C-6, and two stereoselective allylboration reactions to generate the stereocenters at C-2, C-3, C-4, and C-5.

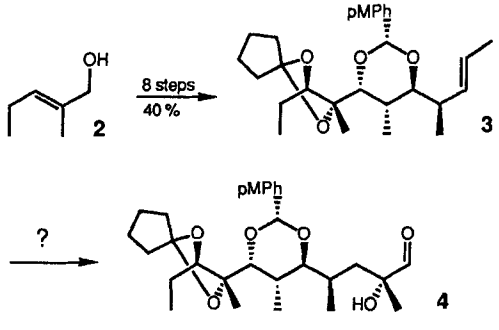
We described in the preceding paper[1] the synthesis of two building blocks for erythronolide A comprising the sequences of stereocenters from C-2 to C-5 and from C-8 to C-13. Difficulties arose, however, in attempts to join the two erythronolide building blocks to the complete molecular skeleton of (9*S*)-dihydro-erythronolide A (**1**) in a convergent synthesis.



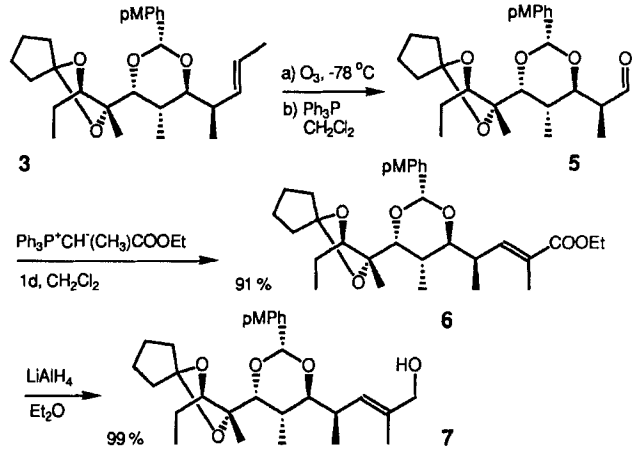
This encouraged us to persue a linear synthesis of (9*S*)-dihydro-erythronolide A (**1**). The success of such a study depends on our ability to create the C-6 stereocenter stereoselectively as well as on the development of suitable deprotection and macrolactonization procedures. In this paper we report on the details of our study, which was completed successfully[2].

The C-6 Stereocenter of Erythronolide A

In our previous studies[1,3] we had synthesized the intermediate **3** in eight steps and 40% overall yield from the alcohol **2**.



For elaboration of the intermediate into the aldehyde **4** with control of the new stereogenic center at C-6 we considered a C-6/C-7 double bond as the prostereogenic element. We therefore converted the alkene **3** into the allylic alcohol **7** by ozonolysis, followed by Wittig olefinantion[4] and subsequent reduction in an overall yield of 91%.



For the introduction of the oxygen function into position C-6 several routes were explored[5]. An epoxidation appeared most attractive in view of the precedent set by Kishi[6] and Thomas[7] with compounds of the type **8**. For instance, the conformation around the C-"7"–C-"8" bond in **8** is governed by allylic 1,3-strain[8] and the benzyloxy group serves as an activating group in the peracid epoxidation. Thus, the high diastereoselectivity reported by Kishi[6] for the epoxidation of **8** is readily rationalized.

It was therefore disappointing that peracid oxidation of the intermediate **7** proceeded without any noticeable asymmetric induction. The *tert*-butyl hydroperoxide/$VO(acac)_2$ epoxidation procedure gave low asymmetric induction in the Kishi system[6] and did not lead to a better result in the case of **7**. It was moreover annoying, that the diastereomeric products **9** and **10** could not be separated by standard chromatography, nor were we able to assign the relative configuration to each of those diastereomers by simple NMR techniques. Fortunately, one diastereomer, **10**, crystallized from the mixture on standing. We therefore resorted

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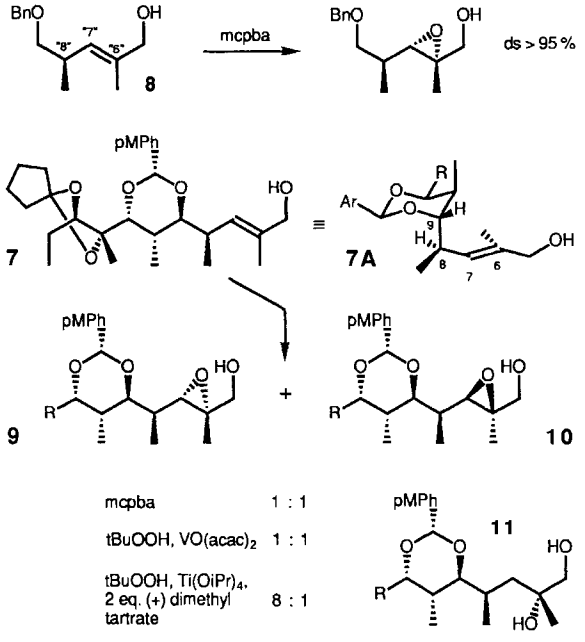
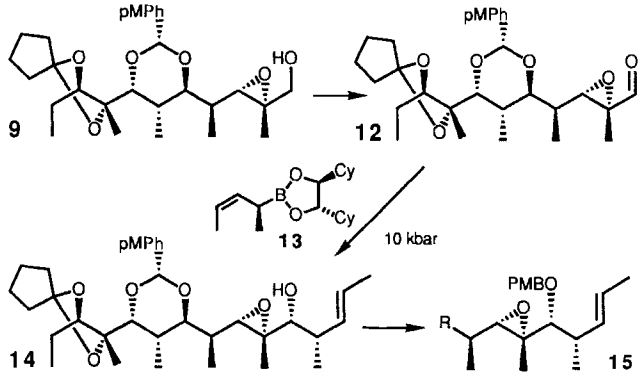
to X-ray crystal structure analysis[9] to establish the configuration at the newly formed stereocenters C-6 and C-7. The crystal structure also gave a hint as to why the epoxidation of **7** had been non-selective. As pointed out elsewhere[1,10], C-8 is in an axial position on the C-9/C-11 dioxane ring. Since C-8 is disubstituted, the C-8–C-9 bond will populate a conformation[11,12] in which 8-H points under the dioxane ring (cf. **7a**). The oxygen atom at C-9 is therefore turned away from the double bond and cannot assist in bringing the peracid to either face of the double bond. The lack of substrate-based asymmetric induction in the epoxidation of **7** is actually a nice confirmation of Kishi's concept[6] of the ether-oxygen-assisted peracid oxidation in the case of **8**.



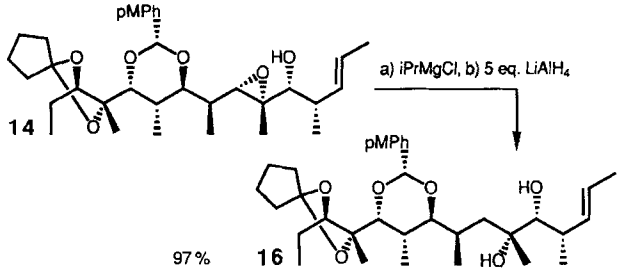
The lack of substrate-based asymmetric induction gives, however, room for reagent controlled asymmetric epoxidation. While the precedent[13] with the Sharpless epoxidation was not encouraging, acceptable levels of diastereoselectivity could be attained by using 2 equivalents of (+)-dimethyl tartrate, 1 equiv. of titanium tetraisopropoxide and 2 equiv. of *tert*-butyl hydroperoxide in CH_2Cl_2. This resulted in a 8:1 diastereomeric mixture of **9** and **10**. Smaller, or larger amounts of dimethyl tartrate, or the use of diethyl or diisopropyl tartrates led to lower diastereoselectivities.

We had not foreseen any problems in the subsequent reductive opening[14] of the epoxide **9** to give the diol **11**. The more we were surprised by the unreactivity of **9** toward $LiAlH_4$, REDAL, DIBAH, DIBAH/$ZnCl_2$, DIBAH/BF_3 or $Ti(OiPr)_4/NaBH_4$. Even up to 10 equiv. of "superhydride"[15], $LiBHEt_3$, failed to react. We were therefore forced to continue our synthesis and hoped that the reductive opening could be realized at a later stage.

To make the situation worse, the oxidation of the primary alcohol **9** to the aldehyde **12** met with difficulties again: Swern oxidation, PCC on alumina, Parikh-Doering oxidation[16], Corey-Kim oxidation[17], or the Dess-Martin periodinane[18] led to extensive decomposition. Eventually, the Ley oxidation with tetrapropyl ammonium perruthenate[19] generated the labile aldehyde **12**, which was immediately treated with the chiral pentenylboronate[13]. Yet, its reaction with the epoxy aldehyde **12** was so slow, that we had to apply high pressure (10 kbar) for 3 d. In this way, the homoallylic alcohol **14** was obtained in 79% overall yield. The sequence of steps was carried out with the 8:1 mixture of **9** and **10**. The undesired C-6/C-7 epimer could then be separated readily at the stage of **14**.



The second assault on reductive opening of the epoxide at the stage of **14** or its *p*-methoxybenzyl derivative **15** failed again with the above-mentioned reagents, as did attempts to open the epoxide by treatment with lithium methylselenolate or lithium phenyltellurolate. Apparently, whatever conformation the epoxide adopts regarding the C-7–C-8 bond (cf. **7a**) either electrophilic activation of the epoxide or nucleophilic attack at the epoxide suffer severe steric hindrance.

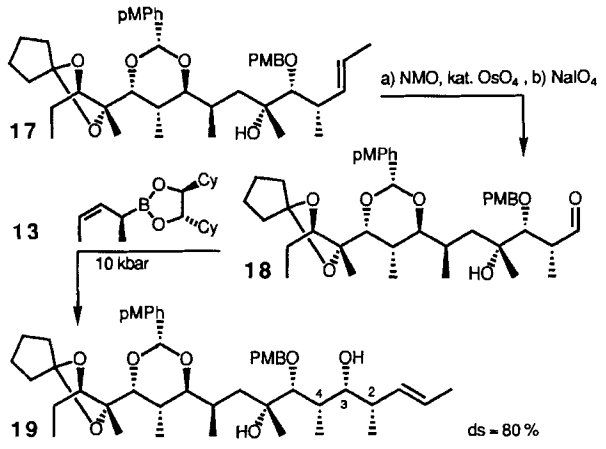


If external electrophilic activation failed, internal activation[20] could be an escape route. Both J. Marshall[21] and D. A. Evans[22] had successfully activated epoxy alcohols towards nucleophilic attack by forming a magnesium alkoxide. Fortunately, reaction of the epoxy alcohol **14** with 1.2 equiv. of isopropylmagnesium bromide followed by 5 equivalents of lithium aluminium hydride, furnished the desired diol **16** in 97% yield. This solved the problem of the C-6 stereocenter.

The Elaboration of the Complete Molecular Skeleton of Erythronolide A

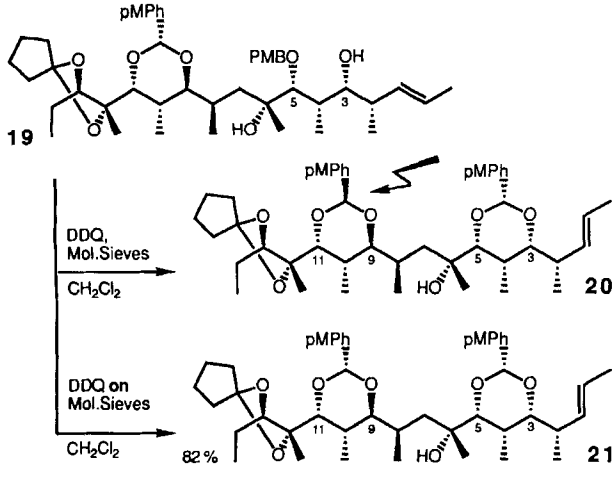
Once, the C-6 stereocenter had been in place, the subsequent steps had already been explored in our studies of the C-1/C-7 building block for erythronolide A[1]. Thus, the secondary hydroxyl group was protected as the *p*-methoxy-

benzyl ether and the double bond was oxidized, this time by bishydroxylation followed by periodate cleavage.



The resulting aldehyde was used immediately in the chain elongation with the chiral pentenylboronate **13** under 10 kbar pressure. The asymmetric induction of the reagent in this reaction is opposite to that of the substrate aldehyde **18** (mismatched pair). Reagent control of stereoselectivity is required to reach the desired configuration at C-2 and C-3. As in our model studies[1] a diastereoselectivity of 80% could be reached. The configuration of the new stereogenic centers was assigned[23] as 2*S*,3*R*, since the major diastereomer contained an *E* double bond. The desired product **19** was thus isolated in 70% overall yield.

Following our model studies the next step was the DDQ oxidation to form the 3,5-*p*-methoxybenzylidene acetal **21**[24]. This turned out much more difficult than anticipated. Ordinary DDQ oxidation led to complete destruction of the substrate. The coproduct of a DDQ oxidation is 2,3-dichloro-5,6-dicyanohydroquinone, a phenol of considerable acidity, which can cause acetal hydrolysis in the presence of traces of water. DDQ oxidation of **19** in rigorously dried (molecular sieves) dichloromethane closed the desired *p*-methoxybenzylidene acetal, yet a closer inspection of the NMR spectra suggested that an epimerization had occurred at the other C-9, C-11 *p*-methoxybenzylidene acetal.

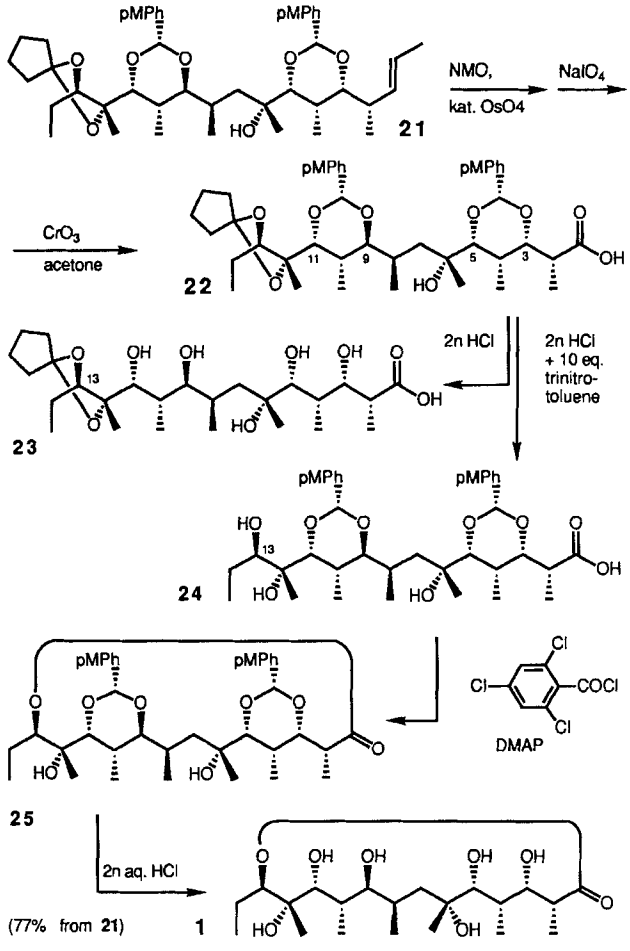


The latter dioxane acetal unit with two axial substituents is highly strained[12] and acid-sensitive. Acidic conditions might therefore cause epimerization at the acetal carbon to a 1,3-dioxane **20** with a twist boat conformation. It has been noted by Stork[25] as well as by Paterson[26], and discussed in detail by Yonemitsu[27] that this epimer is unable to undergo macrolactonization later in the synthesis to give the 14-membered ring. The compound **20** obtained is therefore completely worthless for any synthesis of erythronolide A. Since the dichloro-dicyanohydroquinone is formed as an obligatory coproduct in the DDQ oxidation, it is hard to avoid its acidity. The key is, not to release the hydroquinone into solution. When the oxidation was carried out with DDQ previously coated onto molecular sieves, the C-3/C-5 dioxane ring could be closed without epimerization at the C-9/C-11 dioxane to give the desired **21** in good yield. Apparently, the DDQ and its transformation product, the hydroquinone, do not leave the surface of the molecular sieves.

The Final Macrolactonization to (9*S*)-Dihydroerythronolide A

The tris-acetal **21** contains the full molecular skeleton of erythronolide A as well as all stereogenic centers with the appropriate absolute configuration. In order to reach (9*S*)-dihydro-erythronolide A the plan was to oxidize the double bond to a carboxylic acid, to deprotect the cyclopentylidene acetal, and to effect macrolactonization. Oxidative cleavage of the double bond of **21** was initiated by bishydroxylation with *N*-methylmorpholine *N*-oxide and catalytic amounts of OsO_4, followed by aqueous $NaIO_4$. The aldehyde formed, was oxidized to the carboxylic acid with Jones reagent at −20°C. At these low temperatures even the labile C-9/C-11 acetal survived the acidic conditions. The acid **22** however, resisted isolation: Decomposition ensued on concentration of its solution.

The only product to be identified was anisaldehyde, a sign that the *p*-methoxybenzylidene acetal had been cleaved. This can be ascribed to the intrinsic lability of the C-9/C-11 acetal and the proximity of the carboxy group to the C-3/C-5 acetal unit. In any event, this was a major obstacle, since the plan required that the cyclopentylidene acetal was to be hydrolyzed first to release the C-13 OH group for macrolactonization. Treatment of solutions of the crude acid **22** with either 1N aqueous hydrochloric acid in THF/acetonitrile or with formic acid in aqueous THF reproducibly led to cleavage of the *p*-methoxybenzylidene acetals instead of the cyclopentylidene acetal as desired. The latter had been chosen in the very early stages of our synthesis, because of its facile cleavage under acidic conditions[28]. We had been aware of the fact, that selective cleavage of the cyclopentylidene acetal in the presence of the *p*-methoxybenzylidene acetal was critical. For this reason we had tested[5] early in our synthesis, as soon as we had **3** in our hands, whether this plan could succeed. Treatment of **3** with formic acid in aqueous THF resulted in selective cleavage of the cyclopentylidene acetal. We were therefore struck by the fact that in compound **22** cleavage of the cyclopentylidene acetal turned out to be too sluggish. The consequence,



to introduce another protective group for the C-12/C-13 diol, appeared unacceptable to us, since it implied going back to the second step of the synthesis and starting all over again. Another way of looking at the situation is, to state that the cleavage of the *p*-methoxybenzylidene acetal in **22** is too fast. Of course, the *p*-methoxy group was intentionally chosen to facilitate acetal formation as well as acetal cleavage. The task was therefore, to temporarily interrupt electron release from the electron-rich aromatic system to the acetal carbon. Electron-rich aromatic systems are known to form charge transfer complexes with π-acceptor molecules. We hoped that formation of a charge-transfer complex would deactivate[29] the *p*-methoxyphenyl group sufficiently to allow selective cleavage of the cyclopentylidene acetal. When the crude acid **22** was treated first with 10 equivalents of trinitrotoluene followed by 2M aqueous hydrochloric acid in a two-phase system, indeed the cyclopentylidene acetal could be cleaved selectively. The resulting diol **24** was immediately subjected to the well established Yamaguchi macrolactonization conditions[30] to furnish the bis(*p*-methoxybenzylidene acetal) **25** of (*9S*)-dihydro-erythronolide A. The bis-acetal was characterized by its NMR spectra, which closely corresponded to those of the 3,5-(3,5-dimethoxybenzylidene)-9,11(2,4,6-trimethylbenzylidene) acetal reported by Yonemitsu[10]. 21 of the ^{13}C-NMR signals of the backbone differed by less then 0.5 ppm. In order to obtain (*9S*)-dihydro-erythronolide A (**1**) the deprotection of the *p*-methoxybenzylidene acetals in **25** was immediately effected by 2N aqueous hydrochloric acid. The yield for the six combined operations starting from the alkene **21** was 77% of crystalline material of m.p. 201–203 °C. The mass spectrum agreed with that reported in ref.[10], the ^{1}H-NMR spectrum agreed with the one given in ref.[10,31] and with the spectra kindly provided by Prof. O. Yonemitsu (Sapporo). The ^{13}C-NMR data agreed with a spectrum kindly provided to us by Dr. I. Paterson (Cambridge).

As (*9S*)-dihydro-erythronolide A (**1**) had been converted previously to erythronolide A in three steps[31,32] the attainment of **1** concluded our long-lasting efforts in the erythronolide area. Our synthesis had been undertaken to establish the reliability of stereoselective C–C bond formations using the chiral pentenylboronate **13**[23]. In fact, in the (*9S*)-dihydro-erythronolide A obtained, eight stereogenic centers had been generated by this reagent or its enantiomer. Stereoselectivity in three of the chain elongation steps was >95% and reached in the strongly mismatched case **18** → **19** 80%. It is remarkable that all stereogenic centers of the (*9S*)-dihydro-erythronolide A synthesised by us were generated under reagent-controlled asymmetric induction, be it by the Sharpless epoxidation or the pentenylboronate extension reactions. The efficiency of this process was so high that this linear synthesis of (*9S*)-dihydro-erythronolide A could be realized in 10% total yield over 23 steps with 16 isolated intermediates. Despite being a linear synthesis, this constitutes at present the shortest synthesis of (*9S*)-dihydro-erythronolide A.

We thank the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* for support of this study. R. S. acknowledges gratefully a fellowship by the *Graduierten-Kolleg „Metallorganische Chemie"* at the Philipps-Universität Marburg. We thank in particular Miss *K. Ritter* for her skillful technical assistance. Our thanks go as well to Prof. *D. A. Evans* (Harvard University) for helpful suggestions, to Prof. *O. Yonemitsu* (Sapporo) and Dr. *I. Paterson* (Cambridge) for providing spectra of authentic (*9S*)-dihydro-erythronolide A.

Experimental

All temperatures quoted are not corrected. – ^{1}H NMR, ^{13}C NMR: Bruker AC-300, AM-400, AMX-500. – Boiling range of petroleum ether: 40–60°C. – Flash chromatography: Silica gel Si 60, E. Merck AG, Darmstadt, 40–63 μm. – Analytical gas chromatography: Siemens Sichromat 3 with a 30 m × 0.3 mm quartz capillary column with SE 52, 0.9 bar He.

1. *Ethyl (2E,4R)-4-{(2R,4S,5S,6R)-6-[(2R,3S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-2-methyl-2-pentenoate* (**6**): Into a solution of 1.18 g (2.65 mmol) of (2*R*,3*S*)-2-ethyl-3-{[(2*R*,4*S*,5*S*,6*R*)-2-(4-methoxyphenyl)-5-methyl-4-((1*R*,2*E*)-1-methyl-2-butenyl)]-1,3-dioxan-6-yl}-3-methyl-1,4-dioxaspiro[4.4]nonane (**3**)[1] in 30 ml of CH_2Cl_2 was introduced at −78°C a stream of ozone in oxygen until the blue color persisted. Excess ozone was purged by a stream of nitrogen. 1.05 g (4.0 mmol) of triphenylphosphane was added and the mixture was allowed to reach 0°C. The solvents were removed at 10^{-3} Torr. A small sample of the residue was purified by flash chromatography with petroleum ether/ethyl acetate (10:1) to give

(2*S*)-2-{(2*R*,4*R*,5*S*,6*R*)-6-[(2*R*,3*S*)-2-ethyl-3-methyl-1,4-dioxaspiro-[4.4]nonan-3-yl]-2-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-propanal (**5**). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.4 Hz, 3H), 1.14 (s, 3H), 1.29 (d, *J* = 6.9 Hz, 3H), 1.37 (d, *J* = 6.9 Hz, 3H), 1.55–1.80 (m, 10H), 1.99 (m, 1H), 3.21 (qdd with *J* = 2.8 and 7.0 Hz, 1H), 3.57 (dd, *J* = 9.1 and 3.8 Hz, 1H), 3.79 (s, 3H), 3.83 (d, *J* = 2.1 Hz, 1H), 3.91 (d, *J* = 10.5 Hz, 1H), 5.58 (s, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 2H), 9.60 (d, *J* = 2.9 Hz, 1H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.8, 12.0, 15.2, 22.0, 22.3, 32.1, 24.0, 32.1, 36.7, 38.2, 46.5, 55.2, 75.2, 79.6, 81.5, 87.7, 95.5, 113.5, 117.9, 127.2, 131.2, 159.8, 203.0. – $[\alpha]_D^{20}$ = –8.5 (*c* = 0.4, $CHCl_3$). – $C_{25}H_{36}O_6$ (432.6): calcd. C 69.42, H 8.39; found C 69.25, H 8.41.

The major part of the crude **5** was dissolved in 10 ml of CH_2Cl_2. Then 2.90 g (8.00 mmol) of 1-ethoxycarbonylethylidene-triphenylphosphorane was added. The resulting yellow solution was stirred for 1 d at room temperature. The solvents were removed in vacuo and the residue was purified by flash chromatography with petroleum ether/ether (6:1) to give 1.24 g (91%) of **6** as a viscous oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.4 Hz, 3H), 1.04 (s, 3H), 1.10 (d, *J* = 6.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.19 (d, *J* = 6.8 Hz, 3H), 1.55–1.81 (m, 11H), 1.84 (d, *J* = 1.3 Hz, 3H), 3.38 (m, 1H), 3.46 (d, *J* = 11.0 Hz, 1H), 3.49 (dd, *J* = 7.6 and 4.4 Hz, 1H), 3.74 (s, 3H), 3.76 (d, *J* = 2.1 Hz, 1H), 4.16 (q, *J* = 6.1 Hz, 2H), 5.64 (s, 1H), 6.44 (dd, *J* = 10.0 and 1.4 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.42 8d, *J* = 8.8 Hz, 2H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 12.3, 13.5, 14.4, 15.9, 16.9, 22.1, 23.0, 23.6, 24.5, 31.5, 33.1, 37.3, 38.7, 74.8, 60.8, 76.0, 81.9, 84.9, 88.1, 95.2, 113.8, 118.5, 128.6, 132.4, 143.9, 160.4, 167.5, one signal is obscured by the solvent. – $[\alpha]_D^{22}$ = 37.8 (*c* = 0.70, $CHCl_3$). – $C_{30}H_{44}O_7$ (516.7): calcd. C 69.74, H 8.58; found C 69.54, H 8.32.

2. *(2E,4R)-4-{(2R,4S,5S,6R)-6-[(2R,3S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-2-methyl-2-penten-1-ol* (**7**): 32 mg (0.84 mmol) of $LiAlH_4$ was added at room temperature to a solution of 0.437 g (0.84 mmol) of the ester **6** in 2 ml of ether. After heating to reflux for 6 h 1 ml of ethyl acetate was added. The suspension was stirred with 5 ml of saturated aqueous potassium/sodium tartrate. The mixture was stirred until the solids had dissolved. The phases were separated and the aqueous phase was extracted three times with 20 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. Residual solvents were removed at 10^{-3} Torr to leave 0.394 g (99%) of **7** as a colorless sticky foam. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.4 Hz, 3H), 1.27 (d, *J* = 6.0 Hz, 3H), 1.28 (s, 3H), 1.49 (d, *J* = 6.9 Hz, 3H), 1.77–1.96 (m, 11H), 1.89 (d, *J* = 1.4 Hz, 3H), 2.16 (m, 1H), 3.51 (dq, *J* = 9.5 and 6.2 Hz, 1H), 3.59 (d, *J* = 10.7 Hz, 1H), 3.74 (dd, *J* = 9.7 and 4.3 Hz, 1H), 3.97 (s, 3H), 4.02 (d, *J* = 2.2 Hz, 1H), 4.19 (broad s, 2H), 5.33 (dq, *J* = 9.7 and 1.2 Hz, 1H), 5.87 (s, 1H), 7.07 (d, *J* = 8.7 Hz, 2H), 7.65 (d, *J* = 8.7 Hz, 2H). – ^{13}C NMR (75 MHz, C_6D_6, erythronolide numbering): δ = 12.2 (C-15), 14.3 (6-CH_3), 16.0 (8-CH_3), 17.8 (10-CH_3), 22.2 (12-CH_3), 22.9 (C-14), 23.5, 24.4, 30.7 (C-10), 31.5 (C-8), 37.2, 38.7, 54.7, 68.2 (C-5), 75.9 (C-9), 81.9 (C-12), 85.8 (C-11), 88.1 (C-13), 95.1, 113.7, 118.4, 128.4 (C-7), 132.6, 135.7 (C-6), 160.2, one signal obscured by the solvent. – $[\alpha]_D^{20}$ = 32.7 (*c* = 0.80, $CHCl_3$). – $C_{28}H_{42}O_6$ (474.6): calcd. C 70.86, H 8.92; found C 70.60, H 8.83.

3. *(2S,3S,4S)-2,3-Epoxy-4-{(2R,4S,5S,6R)-6-[(2R,3S)-2-ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-2-methyl-1-pentanol* (**9**): A solution of 0.55 g (1.2 mmol) of **7** in 5 ml of CH_2Cl_2 was added dropwise at –30°C to a cold solution of 0.40 g (2.26 mmol) of (+)-dimethyl tartrate and 0.28 g (1.00 mmol) of titanium tetraisopropoxide in 20 ml of CH_2Cl_2. Then 1.0 g of molecular sieves (3 Å) was added and the mixture was stirred for 10 min. 0.21 g (2.32 mmol) of a 60% solution of *tert*-butyl hydroperoxide in CH_2Cl_2 was added dropwise. The mixture was allowed to stand for 30 h at –28°C. After warming to 0°C 1 ml of dimethyl sulfide was added and after 30 min at 0°C 0.29 g (2.00 mmol) of triethanolamine. The mixture was stirred for 10 min, 10 ml of water was added and the phases were separated. The aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Flash chromatography with petroleum ether/ethyl acetate/triethylamine (3:1:0.01) furnished 0.51 g (90%) of a 8:1 mixture of the epoxides **9** and **10** as a colorless, sticky foam. – $C_{28}H_{42}O_7$ (490.6): calcd. C 68.54, H 8.63; found C 68.73, H 8.59.

9: ^{1}H NMR (400 MHz, C_6D_6): δ = 1.07 (s, 3H), 1.09 (t, *J* = 7.4 Hz, 3H), 1.13 (s, 3H), 1.38 (d, *J* = 6.5 Hz, 3H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.64 (m, 1H), 1.75–1.95 (m, 9H), 2.17 (m, 3H), 2.56 (d, *J* = 9.3 Hz, 1H), 3.72 (AB system, *J* = 11.8 Hz, 2H), 3.27 (s, 3H), 3.52 (dd, *J* = 10.2 and 1.2 Hz, 1H), 3.56 (dd, *J* = 9.5 and 3.5 Hz, 1H), 3.69 (d, *J* = 2.5 Hz, 1H), 5.58 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H). – ^{13}C NMR (75 MHz, C_6D_6, erythronolide numbering): δ = 12.0 (C-15), 13.7 (6-CH_3), 14.7 (10-CH_3), 15.5 (8-CH_3), 22.4 (12-CH_3), 22.8 (C-14), 23.5, 24.4, 31.5 (C-10), 31.7 (C-8), 37.2, 38.7, 54.7, 62.2 (C-6), 64.0 (C-5), 66.4 (C-7), 75.7 (C-9), 81.9 (C-12), 83.5 (C-11), 88.1 (C-13), 95.5, 113.8, 118.5, 128.0, 132.3, 160.3.

The following signals of the minor isomer **10** could be recorded: ^{1}H NMR (400 MHz, C_6D_6): δ = 1.06 (s, 3H), 1.09 (t, *J* = 7.4 Hz, 3H), 1.13 (s, 3H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.69 (d, *J* = 7.0 Hz, 3H), 1.62–1.95 (m, 10H), 2.22 (m, 3H), 2.47 (d, *J* = 9.0 Hz, 1H), 3.27 (s, 3H), 3.28 (AB system, *J* = 11.5 Hz, 2H), 3.62 (dd, *J* = 9.1 and 3.5 Hz, 1H), 3.64 (broad d, *J* = 11 Hz, 1H), 3.92 (d, *J* = 2.0 Hz, 1H), 5.76 (s, 1H), 6.83 (m, 2H), 7.76 (m, 2H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 12.4, 14.1, 14.5, 15.7, 22.2, 23.2, 24.1, 24.4, 31.1, 32.0, 36.7, 38.2, 54.7, 60.2, 62.3, 66.0, 75.3, 81.5, 86.2, 88.1, 95.4, 113.8, 118.3, 128.0, 132.5, 160.4. Eventually, a sample of **10** could be crystallized from benzene/diisopropyl ether, m.p. 83–84°C.

4. *(2E,4S,5R,6S,7S)-6,7-Epoxy-8-{(2R,4R,5S,6S)-6-[(2R,3S)-2-ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-5-hydroxy-4,6-dimethyl-2-nonene* (**14**): To a solution of 0.45 g (0.92 mmol) of **9** in 20 ml of CH_2Cl_2 were added 0.5 g of freshly ground molecular sieves (3 Å) and 0.16 g (1.4 mmol) *N*-methylmorpholine *N*-oxide. After stirring for 0.5 h the mixture was cooled to 0°C and 16.2 mg (0.046 mmol) of tetrapropylammonium perruthenate was added. After stirring for 0.5 h the mixture was filtered with ether over a 4-cm layer of silica gel. The filtrates were concentrated in vacuo and the resulting 0.43 g (96%) of the crude aldehyde **12** was dissolved in 8 ml of petroleum ether. After addition of 0.33 g (1.1 mmol) of (4*S*,5*S*)-4,5-dicyclohexyl-2-((1*S*,2*Z*)-1-methyl-2-butenyl)-1,3,2-dioxaborolane (**13**) the mixture was pressurized for 3 d at 10 kbar. After addition of 0.15 g (1.0 mmol) of triethanolamine the solution was heated to reflux for 1 h. 10 ml of a saturated aqueous NH_4Cl solution were added, the phases were separated and the aqueous phase was extracted three times with 10 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (1:1:0.01) furnished 0.36 g (78%) of the alcohol **14** as a sticky foam. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.3 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 1.21 (s, 3H), 1.31 (s, 3H), 1.39 (d, *J* = 7.0 Hz, 3H), 1.62 (dd, *J* = 6.5 and 1.4 Hz, 3H), 1.50–1.85 (m, 10H), 2.28 (m,

1H), 2.47 (d, J = 8.9 Hz, 1H), 2.75 (d, J = 9.2 Hz, 1H), 2.78 (dd, J = 9.7 and 3.1 Hz, 1H), 3.53 (d, J = 4.7 Hz, 1H), 3.56 (m, 1H), 3.58 (m, 1H), 3.78 (s, 3H), 3.79 (d, J = 2.5 Hz, 1H), 5.20 (ddq, J = 15.2, 8.7, and 1.5 Hz, 1H), 5.49 (dq, J = 15.3 and 6.5 Hz, 1H), 5.62 (s, 1H), 6.85 (d, J = 8.7 Hz, 2H), 7.44 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 12.0, 13.4, 15.4, 18.1, 18.2, 22.3, 22.4, 23.2, 24.1, 30.7, 32.0, 36.8, 38.3, 40.6, 55.3, 62.6, 65.7, 75.2, 81.7, 82.1, 86.1, 87.8, 94.8, 113.5, 117.8, 125.9, 127.3, 131.9, 132.9, 159.7. – $C_{33}H_{50}O_7$ (558.7): calcd. C 70.93, H 9.02; found C 70.91, H 9.25.

5. *(2E,4S,5R,6R,7S,8R)-6,7-Epoxy-8-{(2R,4R,5S,6S)-6-[(2R,3S)-2-ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxybenzyl)-5-methyl-1,3-dioxan-4-yl]}-5-(4-methoxybenzyloxy)-4,6-dimethyl-2-nonene* (**15**): To a suspension of 13.5 mg (0.44 mmol) of sodium hydride (80% in white oil) in 1 ml of dimethylformamide were added 42.0 mg (0.27 mmol) of 4-methoxybenzyl chloride and 50.0 mg (0.089 mmol) of the epoxy alcohol **14** in 1 ml of dimethylformamide. The mixture was stirred for 2 d at room temperature and subsequently hydrolyzed by pouring it onto 1 g of ice. The phases were separated and the aqueous phase was extracted three times with 10 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (8:1:0.01) furnished 40.7 mg (76%) of **15** and 6.1 mg of the 6,7-epimeric epoxide.

15: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.2 Hz, 3H), 0.98 (d, J = 7.1 Hz, 3H), 1.18 (s, 3H), 1.19 (d, J = 7.6 Hz, 3H), 1.28 (s, 3H), 1.34 (d, J = 7.0 Hz, 3H), 1.54 (d, J = 6.4 Hz, 3H), 1.48–1.82 (m, 10H), 1.93 (m, 1H), 2.25 (m, 1H), 2.50 (d, J = 9.7 Hz, 1H), 3.51 (dd, J = 13.0 and 4.9 Hz, 1H), 3.52 (m, 1H), 3.72 (s, 3H), 3.73 (s, 3H), 3.77 (d, J = 1.5 Hz, 1H), 4.38 and 4.69 (AB-system, J = 11.2 Hz, 2H), 5.12 (ddq, J = 15.2, 8.6, and 1.5 Hz, 1H), 6.37 (dq, J = 15.2 and 6.3 Hz, 1H), 5.60 (s, 1H), 6.78 (d, J = 8.8 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.8 Hz, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.7, 12.1, 13.7, 15.4, 18.1, 19.0, 22.2, 22.4, 23.2, 24.0, 30.6, 32.1, 36.8, 38.3, 41.0, 55.3 (2 C), 61.6, 61.8, 72.2, 75.2, 81.7, 86.3, 87.7, 88.5, 94.8, 113.5, 113.6, 117.8, 125.4, 131.1, 129.4, 129.6, 131.9, 133.3, 159.1, 159.6. – The following signals of the C6,C7 epimer could be recorded: δ = 11.4, 11.8, 13.6, 13.9, 22.7, 29.7, 38.2, 39.1, 61.0, 71.4, 87.9, 88.4, 113.8, 125.5, 129.4, 131.1.

6. *(2E,4R,5R,6R,8R)-8-{(2R,4R,5S,6S)-6-[(2R,3S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-5,6-dihydroxy-4,6-dimethyl-2-nonene* (**16**): 1.71 ml (0.60 mmol) of a 0.35 M solution of isopropylmagnesium bromide in THF were added dropwise to a solution of 0.270 g (0.48 mmol) of **14** in 5 ml of anhydrous THF. After stirring for 30 min 0.091 g (2.40 mmol) of $LiAlH_4$ was added and the mixture was held for 6 h under reflux. After cooling excess of $LiAlH_4$ was destroyed by addition of 1 ml of ethyl acetate. 2 ml of water was added, the phases were separated and the aqueous phase was extracted five times with 10 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated to leave 261 mg (97%) of the diol **16** as a sticky resin. – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.00 (t, J = 7.5 Hz, 3H), 1.03 (d, J = 6.8 Hz, 3H), 1.07 (d, J = 6.6 Hz, 3H), 1.11 (s, 3H), 1.18 (s, 3H), 1.30 (d, J = 7.0 Hz, 3H), 1.64 (d, J = 5.5 Hz, 3H), 1.56–1.81 (m, 11H), 1.88 (q, J = 7.6 Hz, 1H), 1.97 (dd, J = 14.5 and 6.5 Hz, 1H), 2.22 (broad s, 1H), 2.37 (sext., J = 6.0 Hz, 1H), 2.48 (m, 1H), 3.20 (broad s, 1H), 3.21 (d, J = 4.2 Hz, 1H), 3.52 (dd, J = 8.8 and 4.2 Hz, 1H), 3.76 (m, 1H), 3.75 (s, 3H), 3.88 (d, J = 8.0 Hz, 1H), 5.42 (ddq, J = 15.5 and 6.8 Hz, 1H), 5.47 (dq, J = 15.7 and 5.6 Hz, 1H), 5.60 (s, 1H), 6.84 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 8.7 Hz, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$, erythronolide numbering): δ = 11.8 (C-15), 15.4 (10-CH_3), 15.6 (4-CH_3), 17.9, 19.5 (8-CH_3), 22.0 (6-CH_3), 22.1 (12-CH_3), 22.3 (C-14), 23.1, 23.9, 26.6 (C-10), 29.1 (C-8), 36.7, 38.2, 38.6 (C-7), 43.5 (C-4), 55.2, 74.9 (C-9), 79.7 (C-5), 81.7 (C-6 + C-12), 85.7 (C-11), 87.8 (C-13), 94.8, 113.4, 117.7, 125.2, 127.2, 132.0, 135.2 (C-3), 159.5. – $C_{33}H_{52}O_7$ (560.7): calcd. C 70.68, H 9.34; found C 70.39, H 9.09.

7. *(2E,4S,5R,6R,8R)-8-{(2R,4R,5S,6S)-6-[(2R,2S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-6-hydroxy-5-(4-methoxybenzyloxy)-4,6-dimethyl-2-nonene* (**17**): A solution of 115 mg (0.20 mmol) of **16** in 3 ml of DMF and subsequently 36 mg (0.23 mmol) of 4-methoxybenzyl chloride were added to a suspension of 18 mg (0.61 mmol) of sodium hydride (80% in white oil) in 2 ml of dimethylformamide. The mixture was stirred for 1 d and was subsequently poured onto 1 g of ice. The phases were separated and the aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (8:1:0.01) furnished 101 mg (72%) of **17** as a viscous oil. – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.0 Hz, 3H), 0.99 (s, 3H), 1.03 (d, J = 6.5 Hz, 3H), 1.05 (d, J = 7.5 Hz, 3H), 1.13 (s, 3H), 1.28 (d, J = 7.0 Hz, 3H), 1.60 (d, J = 5.6 Hz, 3H), 1.48–1.82 (m, 11H), 1.91 (m, 2H), 2.16 (broad s, 1H), 2.43 (m, 1H), 3.01 (d, J = 4.8 Hz, 1H), 3.15 (d, J = 10.8 Hz, 1H), 3.46 (dd, J = 9.8 and 2.9 Hz, 1H), 3.73 (s, 3H), 3.74 (s, 3H), 3.85 (d, J = 1.75 Hz, 1H), 4.36 and 4.59 (AB system, J = 10.7 Hz, 2H), 5.40 (m, 2H), 5.54 (s, 1H), 6.80 (d, J = 8.6 Hz, 4H), 7.18 (d, J = 8.6 Hz, 2H), 7.40 (m, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.9, 15.7, 16.4, 17.9, 19.8, 22.0, 22.3, 22.6, 23.2, 24.0, 26.1, 28.9, 36.8, 38.3, 38.7, 43.1, 55.3 (2 C), 71.4, 75.0, 75.3, 81.8, 86.3, 87.9, 89.5, 94.6, 113.4, 113.9, 117.7, 124.3, 127.2, 129.4, 130.5, 132.2, 132.3, 159.3, 159.5. – $C_{41}H_{60}O_8$ (680.9): calcd.C 72.32, H 8.88; found C 72.14, H 9.05.

8. *(2E,4S,5R,6S,7R,8R,10R)-10-{(2R,4R,5S,6S)-6-[(2R,3S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]}-5,8-dihydroxy-7-(4-methoxybenzyloxy)-4,6,8-trimethyl-2-undecene* (**19**): 67 mg (0.58 mmol) of *N*-methylmorpholine *N*-oxide and 64 mg (0.01 mmol) of a 4% solution of OsO_4 in *tert*-butyl alcohol were added sequentially to a solution of 0.30 g (0.44 mmol) of **17** in 5 ml of acetone. The mixture was stirred for 10 h at room temperature. About 100 mg of Na_2SO_3 was added, followed by 10 ml of water and 20 ml of ether. The phases were separated and the aqueous phase was extracted three times with 20 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. The oily residue was taken up in 5 ml of THF and 5 ml of water and the solution cooled to 0°C. Then 0.12 g (0.56 mmol) of $NaIO_4$ was added and the mixture was stirred for 3 h at 0°C. The phases were separated and the aqueous phase was extracted three times with 20 ml each of ether. The combined organic phases were dried quickly over Na_2SO_4 and concentrated at 0°C in vacuo. The crude aldehyde was immediately dissolved in 8 ml of petroleum ether. 184 mg (0.60 mmol) of (4*S*,5*S*)-4,5-dicyclohexyl-2-((1*S*,2*Z*)-1-methyl-2-butenyl)-1,3,2-dioxaborolane (**13**) was added and the mixture was pressurized for 3 d at 10 kbar. Then 0.15 g (1.0 mmol) of triethanolamine was added and the mixture was heated for 1 h at reflux. 10 ml of saturated aqueous NH_4Cl solution was added, the phases were separated and the aqueous phase was extracted three times with 15 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine

(8:1:0.01) furnished 228 mg (70%) of **19** and 32 mg of a mixture of diastereomeric compounds.

19: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H), 1.04 (d, *J* = 6.5 Hz, 3H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.25 (d, *J* = 6.9 Hz, 3H), 1.43 (s, 3H), 1.53 (s, 3H), 1.59 (dd, *J* = 6.4 and 1.5 Hz, 3H), 1.54–1.89 (m, 12H), 1.95 (m, 1H), 2.26 (m, 2H), 2.30 (m, 1H), 2.39 (m, 1H), 3.16 (d, *J* = 10.1 Hz, 1H), 3.31 (dd, *J* = 9.9 and 2.9 Hz, 1H), 3.50 (m, 1H), 3.55 (d, *J* = 4.7 Hz, 1H), 3.60 (m, 1H), 3.77 (s, 3H), 3.79 (s, 3H), 4.37 and 4.40 (AB system, *J* = 10.5 Hz, 2H), 5.15 (ddq, *J* = 15.3, 8.8, and 1.5 Hz, 1H), 5.47 (dq, *J* = 15.2 and 6.4 Hz, 1H), 5.52 (s, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H). – ^{13}C NMR (125 MHz, $CDCl_3$, erythronolide numbering): δ = 8.0 (4-CH_3), 12.3 (C-15), 15.9 (2-CH_3), 18.1 (10-CH_3), 18.2, 18.5 (8-CH_3), 21.5 (6-CH_3), 22.1 (C-14), 22.4 (12-CH_3), 23.1, 24.0 (C-10), 26.4 (C-4), 29.5 (C-8), 30.0, 36.0, 36.8, 38.9 (C-7), 41.6 (C-2), 55.3 (2 C), 64.2, 75.1 (C-3), 78.6 (C-9), 79.0 (C-5), 81.3 (C-12), 81.7 (C-6), 85.8 (C-11), 87.9 (C-13), 94.8, 113.4, 113.8, 117.7, 125.3, 128.5, 129.2, 129.4, 131.3, 133.3 (C-1), 159.1, 159.5. – $C_{44}H_{66}O_9$ (739.0): calcd. C 71.51, H 9.00; found C 71.80, H 8.86.

9. *(2R,4R)-4-{(2R,4R,5S,6S)-6-[(2R,3S)-2-Ethyl-3-methyl-1,4-dioxaspiro[4.4]nonan-3-yl]-4-[2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl}-2-{(2R,4R,5S,6R)-2-[2-(4-methoxyphenyl)-5-methyl-4-[(2E,S)-2-penten-4-yl]-1,3-dioxan-2-yl]}-2-pentanol* (**21**): 30.0 mg (40.6 μmol) of **9** was dried by twice by distilling 5 ml of benzene from the material and subsequently dissolved in 2 ml of anhydrous CH_2Cl_2. To a solution of 9.5 mg (42 μmol) of dichlorodicyanoquinone in $CHCl_3$ was added 0.2 g of molecular sieves (3 Å). The solution was evaporated to dryness in vacuo and the coated molecular sieves were added at −20°C to the solution of **19** prepared above. Stirring was continued for 6 h at −20°C. Then 200 μl of triethylamine and 3 ml of water were added, the phases were separated and the aqueous phase was extracted three times with 10 ml each of CH_2Cl_2. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. Flash chromatography of the residue with petroleum ether/ethyl acetate/triethylamine (10:1:0.01) furnished 24.5 mg (82%) of **21** as a colorless oil. – ^{1}H NMR (500 MHz, C_6D_6): δ = 1.16 (d, *J* = 6.9 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.31 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.42 (d, *J* = 6.8 Hz, 3H), 1.48 (s, 3H), 1.52 (d, *J* = 7.2 Hz, 3H), 1.72 (dd, *J* = 6.6 and 1.1 Hz, 3H), 1.65–1.82 (m, 15H), 2.40 (m, 1H), 3.19 (s, 3H), 3.32 (s, 3H), 3.35 (d, *J* = 11.8 Hz, 1H), 3.46 (dd, *J* = 8.9 and 4.1 Hz, 1H), 3.74 (d, *J* = 1.9 Hz, 1H), 3.99 (dd, *J* = 10.5 and 2.2 Hz, 1H), 4.17 (broad s, 1H), 5.26 (ddq, *J* = 15.1 and 8.2 Hz, 1H), 5.42 (dq, *J* = 15.1 and 6.6 Hz, 1H), 5.79 (s, 1H), 6.01 (s, 1H), 6.71 (m, 2H), 6.89 (m, 2H), 7.28 (m, 2H), 7.44 (m, 2H). – $C_{44}H_{64}O_9$ (737.0): calcd. C 71.71, H 8.75; found C 71.42, H 8.82.

10. *(9S)-3,5;9,11-Bis(4-methoxybenzylidene)dihydro-erythronolide A* (**25**): To a solution of 32.0 mg (43 μmol) of **21** in 0.5 ml of acetone were added at 0°C 10.5 mg (90 μmol) of *N*-methylmorpholine *N*-oxide and ca. 10 μl of a 4% solution of OsO_4 in *tert*-butyl alcohol. After stirring for 30 min, the solvents were removed i.vac. and the residue was taken up in 1 ml of THF. A solution of 26.0 mg (0.12 mmol) of $NaIO_4$ in 1 ml of water was added, the mixture was stirred for 10 min, the phases were separated and the aqueous phase was extracted three times with 5 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo, the temperature being not allowed to exceed 30°C. The residue was dissolved in 1 ml of acetone and the obtained solution was cooled to −20°C. 100 μl (0.5 mmol) of a 0.5 M solution of Jones reagent in acetone was added dropwise. After stirring for 1 min at −20°C 0.1 ml of 2-propanol was added to stop the reaction. The mixture was immediately filtered over a 1-cm layer of silica gel with ethyl acetate. The filtrate was concentrated at 0°C to about 0.5 ml. 1 ml of methanol, 2 ml of CH_2Cl_2, 120 mg (0.53 mmol) of 2,4,6-trinitrotoluene and 0.5 ml of 2 M aqueous HCl were added sequentially. The mixture was stirred for 30 min at 35°C. All volatile components were removed at 0°C in vacuo and the residue was taken up in 5 ml of toluene. The solution was dried with $MgSO_4$. 12.5 mg (0.1 mmol) of 4-(dimethylamino)pyridine and 11.7 mg (0.5 mmol) of 2,4,6-trichlorobenzoyl chloride was added and the mixture stirred for 1 h at room temperature. This solution was added over a 6-h period by a motor-driven syringe into a refluxing solution of 12.5 mg (0.1 mmol) of 4-(dimethylamino)pyridine in 30 ml of toluene. The solvents were removed i.vac. and the residue of **25** was characterized by the following spectral data: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.4 Hz, 3H), 1.16 (s, 3H), 1.17 (d, *J* = 6.4 Hz, 3H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.32 (s, 3H), 1.40 (d, *J* = 6.6 Hz, 3H), 1.43 (m, 1H), 1.52 (d, *J* = 14.7 Hz, 1H), 1.81 (q, *J* = 6.4 Hz, 1H), 1.85 (m, 1H), 1.92 (m, 1H), 2.38 (s, 1H), 2.47 (m, 1H), 2.66 (s, 1H), 2.90 (dq, *J* = 11.0 and 6.5 Hz, 1H), 3.32 (d, *J* = 11.0 Hz, 1H), 3.70 (s, 1H), 3.81 (d, *J* = 1.2 Hz, 1H), 3.82 (2 s, 3H each), 3.91 (d, *J* = 11.0 Hz, 1H), 4.05 (broad s, 1H), 5.17 (dd, *J* = 11.2 and 2.2 Hz, 1H), 5.66 (s, 1H), 5.75 (s, 1H), 6.90 (d, *J* = 8.7 Hz, 4H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.0, 10.4, 13.9, 14.7, 15.1, 17.2, 20.7, 27.1, 28.5, 29.4, 32.1, 39.8, 41.8, 55.3, 55.4, 74.0, 74.6, 76.7, 77.3, 84.6, 86.3, 87.0, 95.7, 103.4, 113.7 (2 C), 127.6, 127.7, 130.7, 131.1, 160.2 (2 C), 175.3. – $[\alpha]_D^{20}$ = −7.4 (*c* = 0.30, $CDCl_3$).

11. *(9S)-Dihydro-erythronolide A* (**1**): The crude **25** obtained under 10. was taken up in 5 ml of methanol, 2.5 ml of 2 M aqueous hydrochloric acid was added and the mixture was heated for 6 h at 45°C. 10 ml of ethyl acetate was added, the phases were separated and the aqueous phase was extracted five times with 5 ml each of ethyl acetate. The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate (1:2) furnished a colorless solid, which was recrystallized from 0.9 ml of hexane and 0.1 ml of CH_2Cl_3 to give 13.5 mg (77%) of **1** as colorless needles of m.p. 201–203°C (cf. ref.[10] 195–199°C; ref.[31] 202–205°C; ref.[32] 202–204°C). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.3 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 3H), 1.19 (broad d, *J* = 15 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.23 (s, 3H), 1.28 (2 d, *J* = 6.7 Hz, 3H each), 1.42 (dd, *J* = 15.0 and 2.1 Hz, 1H), 1.50–1.57 (m, 3H), 1.75 (broad s, 1H), 1.94 (ddq, *J* = 14.5, 7.5, and 1.9 Hz, 1H), 2.04 (broad q, *J* = 7 Hz, 1H), 2.51 (s, 1H), 2.79 (dq, *J* = 10.4 and 6.9 Hz, 1H), 2.89 (s, 1H), 2.95 (broad t, *J* = ca. 8 Hz, 1H), 3.36 (broad s, 1H), 3.41 (d, *J* = 10.2 Hz, 1H), 3.47 (dd, *J* = 4.4 and 1.6 Hz, 1H), 3.85 (broad d, *J* = 10 Hz, 1H), 3.95 (broad s, 1H), 4.24 (d, *J* = 4.4 Hz, 1H), 4.61 (dd, *J* = 11.0 and 1.5 Hz, 1H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 5.5, 11.0, 12.9, 14.5, 15.8, 17.0, 20.9, 26.7, 32.3, 33.8, 36.2, 41.6, 43.6, 70.1, 75.1, 76.0, 78.8, 80.0, 80.4, 83.1, 178.1. – MS: 402 [$M^+ - H_2O$] (0.4), 384 (2.0), 366 (1.6), 327 (4.4), 281 (4.6), 257 (6.7), 223 (16.2), 197 (15.8), 127 (27.6), 97 (35.0), 69 (62.7), 57 (61.8), 43 (100.0). – $[\alpha]_D^{20}$ = +9.2 (*c* = 0.70, CH_3OH) [cf. ref.[10] + 9.2 (*c* = 0.65, CH_3OH); ref.[31] + 9.5 (*c* = 2.00, CH_3OH); ref.[32] + 8.4 (*c* = 1.00, no solvent given)]; $[\alpha]_{365}^{20}$ = +24.3 (*c* = 0.70, CH_3OH) [cf. ref.[31] + 24.1 (*c* = 2.00, CH_3OH)].

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